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08/989,881	12/12/1997	JEN SHEEN	08472/716002	9398

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	26

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/989,881	Applicant(s) SHEEN, JEN	
	Examiner Cynthia Collins	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,24-26,36-46,49 and 50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,24-26,36-46,49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The supplemental amendment filed April 25, 2003, has been entered.

The appeal brief filed April 28, 2003, has been entered.

The finality of the office action mailed March 28, 2002 is withdrawn.

Claims 1-7, 24-26, 36-46 and 49-50 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-7, 24-26, 36-39 and 41-46 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office actions mailed March 28, 2002.

Applicant's arguments filed April 28, 2003, have been fully considered but they are not persuasive.

The claims are drawn to a method for protecting a plant against any environmental stress, including dehydration stress, excess salinity, temperature and multiple stress conditions, by expressing in a transgenic plant cell a substantially pure DNA encoding any calcium dependent protein kinase (CDPK) polypeptide that includes a protein kinase (PK) domain. The claims are also drawn to a substantially pure DNA, including a DNA substantially identical to SEQ ID NO:1, that encodes any CDPK polypeptide that consists essentially of a PK domain and that is

capable of increasing the level of tolerance of a plant to any environmental stress, including dehydration stress, excess salinity, temperature and multiple stress conditions, and to a cell which includes said substantially pure DNA.

The specification describes the use in a transient maize protoplast system of constructs comprising four different *Arabidopsis* CDPKs disclosed in the prior art: ATCDPK1, ATCDPK1a, AK1 and ATCDPK2. ATCDPK1 and ATCDPK1a are described as having 96% amino acid sequence similarity, and AK1 and ATCDPK2 are described as having 78% and 75% amino acid sequence similarity respectively to ATCDPK1. The specification also describes the use in a transient maize protoplast system of constructs comprising four other prior art disclosed *Arabidopsis* protein kinases that are homologous to the ABA-inducible protein kinase PKABA1: ATTPKa, ATPKb, ASKQ and ASK2. Expression of only two of the eight protein kinase constructs, those comprising the highly homologous CDPKs ATCDPK1 and ATCDPK1a, resulted in the transactivation of a stress-inducible HVA1-LUC reporter construct in the transient maize protoplast system (pages 16-20 and Figure 3E). The specification also describes a mutation that eliminates the ATP-binding site of the PK domain of CDPK1 and that abolishes the ability of CDPK1 to transactivate a stress-inducible HVA1-LUC reporter construct in the transient maize protoplast system (page 20 and Figure 4B).

Applicant argues that the written description requirement is satisfied as the specification describes methods for producing plants that are tolerant to an environmental stress (drought), genes encoding polypeptides encoding PK domains, and methods for isolating and identifying DNAs useful for practicing the claimed invention. Applicant points in particular to pages 10-11 and 36-37 of the specification as describing methods for producing stress tolerant plants, pages 16-22 of the specification as describing a stress-signaling expression pathway as well as

expression constructs useful for generating stress tolerant plants, Figure 3 of the specification describing several PK domains, and pages 13-15 describing how to use a maize protoplast system to select for PK domains active in stress signaling. Applicant additionally points to Example 17 of the written description guidelines where the description requirement for claimed mammalian and human cDNA sequences was not satisfied by the disclosed rat cDNA sequence because no structure common to members of the genus was provided by the specification or the prior art, and because post-filing date evidence indicated a lack of structural relationship between the claimed and disclosed sequences. Applicant argues that the requirements for the disclosure of at least a partial structure common to members of the genus and for post-filing date evidence of a structural relationship between members of the genus are satisfied because the specification discloses genes encoding polypeptides having a structural feature common to the genus (the PK domain), and because the post-filing date publication of Saijo et al. (Exhibit B) provides further evidence of the existence of CDPK genes that confer tolerance to multiple environmental stresses and of the structural feature that is common to members of the genus (appeal brief pages 6-8).

The Examiner maintains that the written description requirement is not satisfied as the specification describes only two highly homologous CDPK sequences (ATCDPK1 and ATCDPK1a) obtained from one plant species (*Arabidopsis*) that can transactivate a stress-inducible HVA1-LUC reporter construct in a transient maize protoplast system, one of which (ATPK1) has also been shown to confer drought tolerance to transgenic *Arabidopsis* plants. This does not constitute a representative number of species supporting the description of a genus as broad as DNA sequences encoding any CDPK polypeptide obtained from any source that

consists essentially of a PK domain and that is also capable of increasing the level of tolerance of a plant to any environmental stress or any combination of environmental stresses.

With respect to the disclosure, the Examiner makes note of the fact that of eight different *Arabidopsis* protein kinases tested for their ability to transactivate a stress-inducible HVA1-LUC reporter construct in the transient maize protoplast system, only the two highly homologous CDPK sequences ATCDPK1 and ATCDPK1a were effective. Six of the eight different *Arabidopsis* protein kinases tested, including two other CDPKs, failed to transactivate a stress-inducible HVA1-LUC reporter construct in the transient maize protoplast system, even though all of the protein kinases tested possess a PK domain. Given this observation, it is unclear how, without further qualification, the PK domain alone could be considered the structural feature common to the members genus that supports the description of the genus, as the structural feature common to the members genus that would support the genus description would also be correlated with the function common to the members genus, namely the ability of the expressed protein to increase the level of tolerance of a plant to any environmental stress.

With respect to the post-filing date publication of Saijo et al. (Exhibit B), the Examiner does not dispute that their disclosure of rice plants transformed with the rice calcium dependent protein kinase OsCDPK7 that are tolerant to cold, salt and drought stress indicates that the genus of CDPKs that can increase the level of tolerance of a plant to an environmental stress includes sequences in addition to ATCDPK1 and ATCDPK1a, and that the genus of stresses to which a CDPK can confer stress includes cold and salt in addition to drought, but the Examiner maintains that the genus is not adequately described by the disclosure. The disclosure indicates that not all plant protein kinases, and indeed not all plant calcium dependent protein kinases, would be expected to increase the level of tolerance of a plant to an environmental stress, and the

disclosure does not indicate which particular CDPKs would increase a plant's tolerance to which particular stresses. The claims do not recite any structural features by which CDPKs that increase the level of tolerance of a plant to an environmental stress may be distinguished from CDPKs that do not, or any structural features by which CDPKS that confer tolerance to different particular stresses may be distinguished from one another, and thus they fail to satisfy the written description requirement.

Claims 1-7, 24-26, 36-46 and 49-50 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for producing transgenic plants that are drought tolerant as a result of the overexpression of a transgene encoding the PK domain of AtCDPK1, does not reasonably provide enablement for producing transgenic plants that are tolerant to other environmental stresses, or for methods for producing transgenic plants that are tolerant to environmental stresses as a result of the overexpression of other transgenes encoding other CDPK polypeptides, for the reasons of record set forth in the office actions mailed March 28, 2002.

The claims are drawn to a method for protecting a plant against any environmental stress, including dehydration stress, excess salinity, temperature and multiple stress conditions, by expressing in a transgenic plant cell a substantially pure DNA encoding any CDPK polypeptide that includes a PK domain. The claims are also drawn to a substantially pure DNA, including a DNA substantially identical to SEQ ID NO:1, that encodes any CDPK polypeptide that consists essentially of a protein kinase domain and that is capable of increasing the level of tolerance of a plant to any environmental stress, including dehydration stress, excess salinity, temperature and multiple stress conditions, and to a cell which includes said substantially pure DNA.

The specification discloses the use in a transient maize protoplast system of constructs comprising four different *Arabidopsis* CDPKs disclosed in the prior art: ATCDPK1, ATCDPK1a, AK1 and ATCDPK2. ATCDPK1 and ATCDPK1a are described as having 96% amino acid sequence similarity, and AK1 and ATCDPK2 are described as having 78% and 75% amino acid sequence similarity respectively to ATCDPK1. The specification also discloses the use in a transient maize protoplast system of constructs comprising four other prior art disclosed *Arabidopsis* protein kinases that are homologous to the ABA-inducible protein kinase PKABA1: ATTPKa, ATPKb, ASKQ and ASK2. Expression of only two of the eight protein kinase constructs, those comprising the highly homologous CDPKs ATCDPK1 and ATCDPK1a, resulted in the transactivation of a stress-inducible HVA1-LUC reporter construct in the transient maize protoplast system (pages 16-20 and Figure 3E). The specification also discloses that a mutation that eliminates the ATP-binding site of the PK domain of CDPK1 also abolishes the ability of CDPK1 to transactivate a stress-inducible HVA1-LUC reporter construct in the transient maize protoplast system (page 20 and Figure 4B). Furthermore, the declaration submitted April 14, 2000 by the inventor indicates that expression of the PK domain of AtCDPK1 under the control of a 35S promoter in transgenic *Arabidopsis* plants renders the transgenic plants tolerant to drought stress as compared to nontransformed wild-type plants. The specification does not disclose CDPKs other than ATCDPK1 or ATCDPK1a that function to transactivate stress inducible reporter constructs, or that function to confer tolerance to any particular stress in transgenic plants. The specification also does not disclose stress inducible reporter constructs that can be transactivated under stress conditions other than those that affect HVA1 (drought, salt and temperature).

Guidance for making and using the claimed invention is necessary because it is unpredictable whether expression of a substantially pure DNA encoding any CDPK polypeptide obtained from any source that includes a PK domain would protect a plant against one or more environmental stresses, because small changes in the amino acid structure of a protein, as would be expected to exist between different CDPK polypeptides, could significantly affect the protein's function. While a large number of diverse CDPKs having distinct amino acid sequences are known in the art, Applicant has provided evidence for only one type of CDPK (ATCDPK1) with respect to its ability to confer tolerance to only one type of stress (drought). Additionally, Applicant's own disclosure suggests that not all CDPKs may function to confer stress tolerance in transgenic plants, as the specification indicates that two *Arabidopsis* CDPKs as well as four other *Arabidopsis* protein kinases were unable to transactivate a stress-inducible HVA-1 reporter construct. Accordingly, the specification does not provide sufficient guidance with respect to how, on the basis of CDPK amino acid structure, one skilled in the art could select from among the numerous CDPK sequences available a substantially pure DNA encoding a CDPK polypeptide that would protect a plant against one or more environmental stresses. Without further guidance, one wishing to practice the invention would have to proceed by trial and error experimentation, testing each particular CDPK polypeptide for its ability to protect a plant against one or more environmental stresses.

Guidance for making and using the claimed invention is also necessary because it is unpredictable which particular environmental stress or stresses the expression of a CDPK polypeptide would protect a plant against, because different molecules mediate plant responses to different types of stress, and because molecules that mediate plant stress responses may function in independent as well as overlapping stress response pathways. First, it is well

established that distinct types of molecules are involved in plant responses to different types of stress. For example, the ability of plants to tolerate high temperature is directly related to the accumulation of heat shock proteins, whereas drought resistance in plants is known to be mediated by an increase in the level of abscisic acid.

Second, while it is generally known in the art that a single type of molecule such as a polypeptide may confer resistance to multiple stresses simultaneously, the combination of particular stresses to which any particular polypeptide may confer resistance is unpredictable, because whether a particular protein can effect tolerance to more than one type of stress simultaneously depends on whether or not that protein functions in a pathway common to multiple stresses. For example, Liu et al. teach that two transcription factors, DREB1 and DREB2, function in two separate signal transduction pathways under low temperature and dehydration conditions respectively (The Plant Cell, 1998, Vol. 10, pages 1391-1406). The expression of DREB1 is induced by low-temperature stress, whereas the expression of DREB2 is induced by dehydration and high-salt stress (page 1398 Figure 6). Furthermore, overexpression of DREB1 in transgenic plants induced the expression of rd29A, a gene whose expression is induced by dehydration, high salt and low temperature stress in nontransgenic wild type plants, whereas overexpression of DREB2 did not induce rd29A expression (page 1402 Figure 11). Liu et al.'s observations indicate that plants respond to stress through independent as well as overlapping biochemical pathways. Accordingly, the ability of a particular protein to affect more than one type of particular stress simultaneously would depend on whether that protein functions as part of an independent stress pathway or as part of an overlapping stress pathway.

In the instant case, while a large number of diverse CDPKs are known in the art, Applicant has provided evidence for only one type of CDPK (ATCDPK1) with respect to its

ability to confer tolerance to only one type of stress (drought). Additionally, Applicant's own disclosure suggests that not all CDPKs may function to confer stress tolerance in transgenic plants, as the specification indicates that two *Arabidopsis* CDPKs as well as four other *Arabidopsis* protein kinases were unable to transactivate a stress-inducible HVA-1 reporter construct. Accordingly, the specification does not provide sufficient guidance with respect to how one skilled in the art could select from among the numerous CDPK sequences available a substantially pure DNA encoding a CDPK polypeptide that would protect a plant against an environmental stress other than drought, or against a specific array of defined multiple environmental stresses. Without further guidance, one wishing to practice the invention would have to proceed by trial and error experimentation, testing each particular CDPK polypeptide for its ability to protect a plant against each of the numerous specific environmental stresses plants may be subjected to.

Given the large number of diverse CDPKs having distinct amino acid sequences known in the art, the unpredictability of a substantially pure DNA encoding any CDPK polypeptide obtained from any source protecting a plant against one or more environmental stresses, the unpredictability of a substantially pure DNA encoding any CDPK polypeptide obtained from any source protecting a plant against a specific combination of environmental stresses, and given the lack of guidance as discussed above, it would require undue experimentation for one skilled in the art to practice the full scope of the claimed invention.

Applicant's arguments filed April 28, 2003, have been fully considered but they are not persuasive.

Applicant argues that identifying and using genes that fall within the scope of the claimed invention may be accomplished without undue experimentation. Applicant points in particular to the inventor's declaration submitted April 14, 2000, which indicates that expression of the PK domain of AtCDPK1 under the control of a 35S promoter in transgenic *Arabidopsis* plants renders the transgenic plants tolerant to drought as compared to nontransformed wild-type plants. Applicant argues that the data disclosed in the declaration provide compelling evidence that transgenic plants expressing a polypeptide that includes a PK domain are tolerant to an environmental stress, and that given such evidence there is no reasonable basis for doubting the objective truth of statements regarding the enablement or predictability of the present invention (appeal brief pages 10-11).

With respect to the inventor's declaration submitted April 14, 2000, the Examiner maintains that the data disclosed in the declaration provide compelling evidence only that transgenic plants expressing an AtCDPK1 polypeptide that includes a PK domain are tolerant to drought stress. Such results conform to the disclosure that the expression of ATCDPK1 results in the transactivation of a stress-inducible HVA1-LUC reporter construct in a transient maize protoplast system. The Examiner further maintains that Applicant's own disclosure provides a reasonable basis for questioning the enablement and predictability of other CDPKs functioning to confer stress tolerance when expressed in transgenic plants, as the specification discloses that only two of four different CDPK polypeptides tested, the highly homologous CDPKs ATCDPK1 and ATCDPK1a, resulted in the transactivation of a stress-inducible HVA1-LUC reporter construct in a transient maize protoplast system.

Applicant also argues that the specification provides explicit guidance for identifying and isolating DNA sequences encoding polypeptides having PK domains from a variety of sources, for testing whether constructs comprising isolated DNA sequences encode proteins that activate stress signaling pathways, for transforming plants with isolated DNA sequences encode proteins that activate stress signaling pathways, and for testing transformed plants for stress tolerance. Applicant additionally points out that the basic tools required for isolating DNA sequences and expressing them in plants were known and used in the art at the time of filing, and that the data provided the inventor's declaration submitted April 14, 2000 provides strong evidence that plants expressing a polypeptide having a PK domain have increased tolerance to an environmental stress. (appeal brief pages 11-13).

The Examiner does not dispute that the specification discloses methods for identifying and isolating DNA sequences encoding polypeptides having PK domains, methods for testing whether constructs can activate stress signaling pathways, methods for transforming plants, and methods for testing transformed plants for stress tolerance, or that the basic tools required for isolating DNA sequences and expressing them in plants were known and used in the art at the time of filing. The Examiner maintains that the specification does not provide sufficient guidance for one skilled in the art to discriminate between those CDPK sequences that would confer tolerance to a particular stress when used to transform a plant and those that would not, as the specification indicates that some CDPKs (the highly homologous ATCDPK1 and ATCDPK1a) can transactivate a stress inducible reporter construct, whereas other CDPKs (AK1 and ATCDPK2) cannot. Absent guidance for how to discriminate between the many different CDPK sequences available, it would require undue experimentation to practice the claimed invention, as the effect of each CDPK sequence on every conceivable type of stress that plants are subject to

would have to be tested in order to practice the invention commensurate in scope with the claims. Furthermore, with respect to the inventor's declaration submitted April 14, 2000, the Examiner maintains that the declaration only provides evidence that transgenic plants expressing an AtCDPK1 polypeptide that includes a PK domain are tolerant to drought stress.

Applicant additionally points to the submitted publication of Saijo et al. (Biochimica et Biophysica Acta, 1997, Vol. 1350: 109-114, Exhibit A), coauthored by the inventor, which discloses the cloning of two maize CDPKs using methods disclosed in the specification, and argues that there is no reason to believe that the specification does not enable the identification of additional CDPK genes from any plant without undue experimentation. Applicant also argues that determining whether a particular CDPK provides protection against an environmental stress is easily accomplished by overexpressing the gene in a transgenic plant, and points in particular to the submitted publication of Saijo et al. (Plant Journal, 2000, Vol. 23: 319-327, Exhibit B), which discloses the cloning of a rice CDPK gene OsCDPK7 using the maize CDPK gene ZmCDPK7 disclosed in Saijo et al. Exhibit A, and that the expression of OsCDPK7 in transgenic rice plants confers tolerance to cold, salt and drought stresses. Applicant further argues that Exhibit B provides additional evidence that CDPK genes may be isolated using methods disclosed in the specification, and that. Exhibit B provides evidence that CDPK genes conferring tolerance to multiple stresses may be readily identified without undue experimentation, as plants having increased stress tolerance are easily distinguished from those that do not. Applicant further points out that the methods used in Exhibit B were known in the art at the time of filing, and that the use of post-filing date publications as evidence of the state of the art existing at the time of filing and its relevance to enablement is an accepted practice. (appeal brief pages 13-15).

With respect to Exhibits A and B, the Examiner does not dispute that the methods used in Exhibits A and B were known in the art at the time of filing. The Examiner disagrees, however, that data published post-filing date may be used as evidence of the state of the art existing at the time of filing. The Examiner maintains that data published post-filing date can be used as evidence that the claimed invention was enabled at the time of filing, but only if the post-filing date publication follows exactly the guidance set forth in the specification, and only if the guidance set forth in the specification is very specific. While the specification indicates at page 23 that additional sequences encoding CDPKs that regulate a stress signal transduction response may be isolated by using all or part of a CDPK (described hererin) as a probe to screen a recombinant plant DNA library for genes having sequence identity to the CDPK gene or its PK domain, the maize ZmCDPK7 cDNA used by Saijo et al. (Exhibit B) to isolate the rice clone OsCDPK7 does not appear to be among the CDPKs described in the specification. Accordingly, the data published post-filing date does not constitute evidence that the claimed invention was enabled at the time of filing.

The Examiner also maintains that the specification does not provide sufficient guidance for one skilled in the art to discriminate between those CDPK sequences that would confer tolerance to a particular stress when used to transform a plant and those that would not, as discussed *supra.* Exhibit B does not overcome the enablement rejection in this respect, as the specification does not provide any guidance for identifying, prior to its testing, OsCDPK7, or any other CDPK, as a CDPK that would confer tolerance to a specific stress when expressed in a transgenic plant. The Examiner also disagrees with the assertion that determining whether a particular CDPK provides protection against an environmental stress is easily accomplished. Given that some CDPKs would provide protection against an environmental stress and others

would not, it is unpredictable whether any particular CDPK would provide protection against any particular environmental stress. Furthermore, given the vast array of abiotic and biotic stresses to which plants are subject and the ability of plants to respond to different stresses through independent pathways, it is unpredictable which stress(es), if any, any particular CDPK would provide protection against. Without further guidance, each particular CDPK would have to be tested for its effect against each particular type of stress in order to determine which stress(es), if any, a particular CDPK could protect a plant against.

Applicant also argues that the Office has not established a reasonable basis to question the enabling nature of the specification, as no scientific evidence currently of record establishes such a basis (appeal brief pages 16-17).

The Examiner disagrees that the Office has not established a reasonable basis to question the enabling nature of the specification. As set forth at page 6 of the office action mailed October 12, 1999, and pages 6-7 of the office action mailed August 7, 2000, enablement was questioned on the basis of the fact that small changes in the amino acid structure of a protein could significantly affect its function. Given the large number of diverse CDPK sequences known in the art, and given the limited disclosure that one of two highly homologous *Arabidopsis* CDPK sequences that can transactivate a stress-inducible HVA1-reporter construct can also confer drought tolerance on transgenic plants, and given the disclosure that two other *Arabidopsis* CDPK sequences cannot transactivate a stress-inducible HVA-1 reporter construct, the fact that small changes in the amino acid structure of a protein could significantly affect its function is evidence of record that establishes a reasonable basis to question the enablement of any or all

CDPK polypeptides functioning to confer tolerance to any stress or any combination of stresses upon expression in a transgenic plant.

Additionally, at pages 7-8 of the office action mailed August 7, 2000, enablement was questioned on the basis of the fact that different types of molecules are known to mediate plant responses to different types of environmental stresses, and on the basis of a correlation between drought stress and the many diverse stresses that fall within the scope of the claims not having been established. Enablement was also questioned on the basis of the fact that the disclosure indicates that the effects of CDPK1 and CDPK1a are specific to these molecules, since six other plant protein kinase having PK domains, including two other plant CDPKs, failed to transactivate the stress-inducible HVA1-reporter construct activated by CDPK1 and CDPK1a. Enablement was additionally questioned on the basis of the fact that high and low temperatures do not induce the expression of two plant CDPKs, ATCDPK1 and ATCDPK2, even though temperature extremes are among the stresses encompassed by the claims, and even though ATCDPK1 and ATCDPK2 are among the CDPK polypeptides encompassed by the claims. These facts also constitute evidence of record that establishes a reasonable basis to question the enablement of any or all CDPK polypeptides functioning to confer tolerance to any stress or any combination of stresses upon expression in a transgenic plant.

Enablement of the full scope of the claimed invention may also be reasonably questioned on other grounds, such as those discussed *supra* with respect to the unpredictability of a polypeptide conferring resistance to multiple stresses simultaneously.

Claim Rejections - 35 USC § 102

Claims 36-46 remain rejected under 35 U.S.C. 102(b) as being anticipated by Urao et al. (Mol. Gen. Genet. 1994, Vol. 244, pages 331-340), for the reasons of record set forth in the office actions mailed March 28, 2002.

The claims are drawn to substantially pure DNA encoding a calcium dependent protein kinase (CDPK) polypeptide consisting essentially of a protein kinase (PK) domain, said polypeptide being capable of increasing the level of tolerance to an environmental stress in a transgenic plant.

Urao et al. teaches the nucleotide and deduced amino acid sequences of the calcium-dependent protein kinases ATDPK1 and ATDPK2, isolated from *Arabidopsis*, which are substantially identical to the nucleotide sequence of SEQ ID NO:1 (Figure 3A,B, page 334).

Applicant's arguments filed April 28, 2003, have been fully considered but they are not persuasive.

Applicant argues that since Urao et al. discloses full length cDNA molecules encoding full length CDPK polypeptides, Urao et al. does not disclose a DNA molecule encoding a PK domain consisting essentially of itself, and thus does not identically describe the claimed subject matter. Applicant further argues that a DNA molecule encoding a PK domain consisting essentially of itself is not inherently disclosed by Urao et al., as one skilled in the art would not interpret or conclude that Urao's disclosure of full-length CDPK molecules was an unequivocal teaching of CDPK fragments, such as the PK domain, having a specific biological activity (appeal brief pages 18-19).

The Examiner maintains that the disclosure of full-length cDNA molecules encoding full-length CDPK polypeptides by Urao et al. does disclose a DNA molecule encoding a PK domain

consisting essentially of itself. The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials (here the PK domain) and those that do not materially affect the basic and novel characteristics of the claimed invention (here the remainder of the CDPK polypeptide) (MPEP 2111.03). "For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising" ... If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention" (MPEP 2111.03). In this respect, The Examiner notes that Applicant's own specification teaches that a plant may be protected against an environmental stress by the expression of recombinant genes encoding a protein kinase domain, a polypeptide substantially identical to the amino acid sequence of ATCDPK1 or ATCDPK1a, or a calcium-dependent protein kinase (see for example page 2 line 20 to page 3 line 18, or page 10 line 23 to page 11 line 6). Given Applicant's disclosure, the presence of amino acids outside of the PK domain of the CDPK polypeptides disclosed by Urao et al. would not appear to materially affect the basic and novel characteristics of the claimed invention.

With respect to Applicant's argument that a DNA molecule encoding a PK domain consisting essentially of itself is not inherently disclosed by Urao et al., the Examiner maintains that the inherency of a PK domain consisting essentially of itself is a property of the polypeptides disclosed by Urao et al., regardless of how one skilled in the art would interpret Urao's disclosure.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
October 1, 2003

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600